REMARKS

Status of the Claims

Claims 1-20, 25-27, 29-40 and 43-57 are pending in the application. Claims 29, 30, 43, 44 and 46-49 are withdrawn. Claims 1-20, 25-27, 31-40, 45 and 50-57 are rejected.

Indefiniteness Rejection

The Office rejects claims 1-20, 25-27, 31-40, 45, and 50-57 under 35 U.S.C. §112, first paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Office objects to the recitation of "antagonizing P-selectin or E-selectin" and alleges that it is a relative term that renders the claims indefinite. Office Action of 09/07/05, p. 3.

Applicants believe that the term "antagonizing" is well understood by the skilled artisan. In an effort to facilitate prosecution, however, the Applicants have deleted the term "antagonizing P-selectin or E-selectin" and respectfully request that the rejection be withdrawn.

Novelty Rejection

The Office maintains the prior rejection of claims 1-4, 8-13, 16-18, 25-27, 45-47, 50-53, and 57 under 35 U.S.C. § 102(e) as allegedly anticipated by Cummings et al., U.S. Patent No. 5,464,778 ("Cummings"), as further evidenced by The Merck Manual of Diagnosis and Therapy (17th ed.) ("Merck Manual"). Cummings allegedly teaches treatment of (1) stroke; (2) atherosclerosis; and (3) ischemia/reperfusion injury. The Office maintains that the cited passages from the Merck Manual "provide evidence that

the prior art targeted conditions and diseases were associated with hypertension." Office Action of 09/07/05, p. 3. The Office further contends that, despite the fact that "prior art targeted patient populations do not necessarily have or develop hypertension, *one of ordinary skill in the art would have immediately envisaged at the time the invention was made* that the prior art treatment of ischemia-reperfusion injury, atherosclerosis, and strokes was targeting patients with hypertension." *Id.* (emphasis added). This is not the proper standard for determining inherency.

The Legal Standard For Determining Inherency

A claim is anticipated "only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." MPEP § 2131 (8th ed., 2d rev. 2004) (citing *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987)). Normally, only a single reference should be used in rejecting an application under 35 U.S.C. § 102, though a § 102 rejection over multiple references has been found proper where the additional reference was cited: (1) to prove the primary reference contains an enabled disclosure; (2) to explain the meaning of a term used in the primary reference; or (3) to show that a characteristic not disclosed in the primary reference is inherent. MPEP § 2131.01. The reference "must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill." MPEP § 2112 (citing *Schering Corp. v. Geneva Pharmaceuticals, Inc.*, 339 F.3d 1373, 1376 (Fed. Cir. 2003)) (emphasis added). Finally, inherency "may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient." MPEP § 2112 (citing In re Robertson, 169 F.3d

743, 745 (Fed. Cir. 1999)). The burden is on the Office to "provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." MPEP § 2112 (citing *Ex parte Levy*, 17 U.S.P.Q.2d 1461, 1464 (Bd. Pat. App. & Inter. 1990)). The Applicants respectfully submit that the Office has failed to meet this initial burden, because it does not rely on a proper standard for determining inherency.

Hypertension is Not Necessarily Associated with the Conditions of Cummings

In its rejection of claims 1-4, 8-13, 16-18, 25-27, 45-47, 50-53, and 57, the Office fails to meet its burden in showing that hypertension is necessarily associated with the conditions of Cummings. The Office cited portions of The Merck Manual that purport to show that hypertension is inherent in the conditions of Cummings. Office Action, 3/17/2005. However, the Merck Manual tends to exemplify the distinct nature of hypertension and the conditions of Cummings. For example, the Merck Manual describes the characteristics of atherosclerotic vessels and then describes the distinct characteristics of such vessels when hypertension is present. THE MERCK MANUAL OF DIAGNOSIS AND THERAPY 1655 (17th ed. 1999). This description indicates that hypertension and atherosclerosis need not coexist. In fact, hypertension is not listed as a symptom characteristic of atherosclerosis in the passage of the Merck Manual cited by the Office, which states that "[a]therosclerosis is characteristically silent until critical stenosis, thrombosis, aneurysm, or embolus supervenes." THE MERCK MANUAL OF DIAGNOSIS AND THERAPY 1657 (17th ed. 1999). Moreover, the Office cites

passages of the Merck Manual that describe hypertension as a "risk factor" for several diseases. Office Action, 9/7/2005, p. 4. For example, the Office quotes the Merck Manual's statement that hypertension is one of "three risk factors, along with cigarette smoking and hypercholesterolemia predisposing to coronary atherosclerosis" and hypertension is the "most important risk factor predisposing to stroke." *Id.* The manner in which they are described indicates that risk factors are factors that may alter the probability or possibility of a particular disease but are not necessarily associated with the disease. The fact that some risk factors are more "important" than others may suggest a stronger association, but not that the risk factor and the disease are necessarily associated. For instance, atherosclerosis can be caused by hypercholesterolemia, and a stroke may be caused by an embolism, as applicants have previously argued. In these instances, hypertension would not be associated with the conditions of Cummings.

The Applicants respectfully submit that the Office has not met its burden for a showing of inherent anticipation because the documents cited by the Office fail to show that hypertension is necessarily present in the diseases in Cummings. The Applicants respectfully request that the rejections of claims 1-4, 8-13, 16-18, 25-27, 45-47, 50-53, and 57 be withdrawn.

Obviousness Rejections

The Office maintains the prior rejection of claims 1-20, 25-27, 31-40, 45, and 50-57 under 35 U.S.C.§ 103(a) as allegedly unpatentable over Cummings and Larsen *et*

al., U.S. Patent No. 5,840,679 ("Larsen") in view of Blann *et al.*, "Evidence of platelet activation in hypertension," *J. Hum. Hyper.* 11:607-609 (1997) ("Blann"), Araneo *et al.*, U.S. Patent No. 6,150,348 ("Araneo") and DeFrees *et al.*, U.S. Patent No. 5,604,207 ("DeFrees"), and further in view of the Merck Manual.

While the Office acknowledges that neither Cummings nor Larsen discloses treating or inhibiting hypertension and deep vein thrombosis ("DVT") by inhibiting the interaction between P-selectin and PSGL-1 *per se*, it alleges that the secondary references of Blann, Araneo, and DeFrees all teach the role of such interactions in various thrombotic conditions, including hypertension and DVT, at the time the invention was made. The Office apparently contends that administration of PSGL-1 to treat the conditions recited in Cummings and Larsen would inherently treat hypertension, and therefore thrombosis.

The Office continues to rely upon an improper finding of inherency. Cummings and Larsen neither teach nor suggest the use of a PSGL-1 protein for treating or inhibiting thrombosis in a patient with hypertension. As noted above, Cummings neither teaches nor suggests that hypertension is necessarily associated with any of the conditions discussed therein. Larson also fails to show such an association. Blann, Araneo, DeFrees and the Merck Manual fail to cure the deficiencies of Cummings and Larsen. First, none of these references teach or suggest that hypertension is necessarily associated with the conditions discussed in Cummings and/or Larsen. Second, each of Blann (the acetylcholinesterase inhibitor quinapril), Araneo (a dehydroepiandrosterone derivative), and DeFrees (analogues of sialyl-Lewis^x) discuss compounds other than a PSGL-1 protein for treating conditions other than thrombosis in

a subject having hypertension. Therefore, the conclusion of the Office that "it would have been inherent that such patients would have been identified as being subjects having hypertension," is not supported by the cited documents. Office Action, 9/7/2005, p. 6. The Applicants respectfully request that the rejection of claims 1-20, 25-27, 31-40, 45, and 50-57 be withdrawn.

The Office maintains the prior rejection of claim 27 under 35 U.S.C.§ 103(a) as allegedly unpatentable over Cummings and Larsen, in view of Blann, Araneo, DeFrees, the Merck Manual, as applied to claims 1-20, 25-27, 31-40, 45, and 50-57 above, and further in view of Maugeri *et al.*, "Polymorphonuclear Leukocyte-Platelet Interaction: Role of P-selectin in Thromboxane B_2 and Leukotriene C_4 Cooperative Synthesis," *Thromb. Haem.* 72:450-456 (1994) ("Maugeri") and Johnston *et al.*, "Differential Roles of Selectins and the α4-Integrin in Acute, Subacute, and Chronic Leukocyte Recruitment In Vivo," *J. Immunol.* 159:4514-4523 (1997) ("Johnston").

Claim 27 is directed to a method for inhibiting thrombus formation induced by leukotriene C_4 ("LTC_4") in a subject by identifying a subject at risk of thrombosis resulting from hypertension and administering to the subject a composition comprising an effective amount of soluble PSGL-1 protein or a fragment thereof. The Office conceded that Cummings and Larsen do not disclose the role of LTC_4 in thrombus formation or thrombotic conditions *per se*, but maintains that LTC_4 was a known thrombus-inducing agent involved in thrombus formation and thrombotic conditions, as allegedly shown by Maugeri and Johnston. Office Action of 09/07/05, p. 9.

As noted above, neither Larsen nor Cummings teach or suggest treating or inhibiting thrombosis in a subject with hypertension and Blann, Araneo, DeFrees or the

Merck Manual do not compensate for this deficiency, since none of these documents discuss administering a PSGL-1 protein for treating or inhibiting thrombosis in a subject having hypertension. Similarly, neither Maugeri nor Johnston compensate for these deficiencies because they also fail to discuss treating or preventing thrombosis in a subject having hypertension. Accordingly, the subject matter of claim 27 is not obvious in light of the documents mentioned by the Office, and the Applicants respectfully request that the rejection of claim 27 be withdrawn.

Conclusion

In view of the foregoing remarks, the Applicants respectfully request reconsideration and reexamination of the application and the timely allowance of the pending claims.

Please grant any extensions of time required to enter this response and charge any additional required fees to our deposit account 06-0916.

Respectfully submitted,

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